Diagnostic Value of Neutrophil-to-Lymphocyte Ratio, Serum Interleukin-6 and CRP in Pediatric Tonsillitis

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ABSTRACT
Pediatric tonsillitis is a common condition requiring accurate diagnosis to guide appropriate treatment and prevent complications. Biomarkers such as Neutrophil-to-Lymphocyte Ratio (NLR), Serum Interleukin-6 (IL-6) and C-Reactive Protein (CRP) have shown promise in differentiating bacterial from viral infections, but their diagnostic utility in pediatric tonsillitis remains under explored. To evaluate the diagnostic value of NLR, IL-6, and CRP in distinguishing bacterial from viral tonsillitis in pediatric patients and to analyze their correlation with disease severity. A prospective observational study was conducted at the Department of ENT, Mamata Medical College, in collaboration with the Department of Biochemistry. Fifty pediatric patients aged 5-15 years with a clinical diagnosis of tonsillitis were enrolled. Data on demographic characteristics, clinical history and associated symptoms were collected. NLR, IL-6 and CRP were analyzed. Throat swab cultures were performed to confirm bacterial etiology. Data were analyzed for mean, standard deviation and diagnostic accuracy using Receiver Operating Characteristic (ROC) curves. The study demonstrated that NLR (Mean: 6.8±1.8) was significantly higher in bacterial tonsillitis (8.2) compared to viral cases (5.4). IL-6 levels (Mean: 35.4±8.6 pg/mL) and CRP levels (Mean: 12.8±3.2 mg/L) were also markedly elevated in bacterial infections. Group A Streptococcus was identified in 70% of bacterial cases. NLR and IL-6 showed the strongest diagnostic accuracy, emphasizing their utility as reliable tools for distinguishing bacterial tonsillitis. NLR, IL-6 and CRP are valuable tools for differentiating bacterial from viral tonsillitis in pediatric patients. These biomarkers, alongside microbiological analysis, enhance diagnostic precision and can aid in guiding appropriate treatment strategies. Future research should focus on establishing standardized cutoff values for these markers.

INTRODUCTION

Pediatric tonsillitis, a prevalent upper respiratory tract infection, remains a significant clinical concern due to its overlapping clinical presentation with other oropharyngeal infections, such as viral pharyngitis and streptococcal infections[1]. The difficulty in distinguishing bacterial from viral etiologies complicates treatment decisions, often leading to the overuse of antibiotics. This over prescription not only contributes to the growing global issue of antibiotic resistance but also places unnecessary burdens on healthcare resources. Accurate and early diagnosis is critical for initiating appropriate treatment to prevent potentially serious complications, such as peritonsillar abscess, rheumatic fever and post-streptococcal glomerulonephritis[2]. In this context, biomarkers such as the neutrophil-to-lymphocyte ratio (NLR), serum interleukin-6 (IL-6) and C-reactive protein (CRP) have gained attention for their potential in diagnosing and assessing the severity of inflammatory conditions, including pediatric tonsillitis[3]. NLR, a cost-effective and readily available marker derived from routine blood tests, reflects systemic inflammation and has been explored in various infectious and inflammatory conditions. Similarly, IL-6, a cytokine released during acute and chronic inflammation and CRP, a sensitive acute-phase reactant, are widely recognized indicators of immune system activation during infections[4]. Despite their promise, the diagnostic application of these biomarkers in pediatric tonsillitis remains insufficiently explored. Most existing studies have focused on adult populations or generalized infections, such as pneumonia or sepsis[5]. Their specific roles in differentiating bacterial tonsillitis from viral tonsillitis or predicting disease severity in children are inadequately defined. Moreover, the limited research in pediatric settings leaves a critical gap, as children often present unique physiological and immunological characteristics that may affect biomarker dynamics. Current literature emphasizes the utility of NLR, IL-6, and CRP in generalized inflammatory conditions but offers limited insights into their tailored application for pediatric tonsillitis[6]. This lack of targeted investigations hinders the development of precise diagnostic algorithms essential for pediatric populations. Rapid and non-invasive differentiation between bacterial and viral etiologies in children is particularly vital to minimize unnecessary antibiotic use, reduce healthcare costs and improve patient outcomes[7]. This study aims to address these gaps by evaluating the diagnostic value of NLR, IL-6 and CRP in pediatric tonsillitis. Specifically, the study seeks to analyze the ability of these biomarkers to differentiate between bacterial and viral etiologies, assess disease severity and contribute to the development of evidence-based diagnostic protocols. By focusing on a pediatric cohort, this research aims to bridge the existing knowledge gap, enhance diagnostic accuracy, and guide more effective and individualized treatment strategies, ultimately benefiting patient care and healthcare systems.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of ENT in collaboration with the Department of Biochemistry, Mamata Medical College, Telangana, India. The study was carried out over a period of one year. A total of 50 pediatric patients aged 5-15 years, clinically diagnosed with tonsillitis, were included in the study. The diagnosis was based on clinical findings such as sore throat, fever, swollen tonsils and cervical lymphadenopathy. Patients with chronic tonsillitis, systemic inflammatory conditions, or recent use of antibiotics within two weeks prior to presentation were excluded. The sample size of 50 was determined based on feasibility within the study period and available resources while maintaining statistical reliability for preliminary findings.

Demographic and Clinical History: Detailed demographic data, including age, sex and socioeconomic status, were recorded for each participant. A structured questionnaire was used to obtain the clinical history, which included the following parameters.
- Duration severity of symptoms such as sore throat, fever, odynophagia and dysphagia.
- History of prior episodes of tonsillitis or recurrent infections.
- Family history of similar conditions.
- Associated symptoms, including ear pain, snoring, or obstructive sleep apnea.
- Vaccination status and any recent exposure to infectious agents.

Data Collection:
- **Clinical Assessment:** All patients underwent a thorough ENT examination by specialists, including inspection of the oropharynx and palpation of cervical lymph nodes. The severity of symptoms was recorded using a structured proforma.

- **Laboratory Investigations:** Blood samples (5 mL) were collected under sterile conditions and analyzed for the following parameters.

- **Neutrophil-to-Lymphocyte Ratio (NLR):** Obtained from the complete blood count (CBC) with differential.
- **Serum Interleukin-6 (IL-6):** Measured using enzyme-linked immunosorbent assay (ELISA) kits.
- **C-Reactive Protein (CRP):** Assayed using a high-sensitivity CRP (hs-CRP) analyzer.
- **Microbiological Analysis:** Throat swabs were collected for bacterial culture to identify the causative organism in cases of bacterial tonsillitis. Viral etiologies were inferred in culture-negative cases with clinical features consistent with viral infections.

Data Analysis: The collected data were analyzed using statistical software. Descriptive statistics were used for demographic and clinical variables. NLR, IL-6 and CRP levels were compared between bacterial and viral tonsillitis groups using the independent t-test or Mann-Whitney U test, depending on data distribution. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic accuracy of the biomarkers. A $p < 0.05$ was considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Ethics Committee of Mamata Medical College. Written informed consent was obtained from the parents or guardians of all participants prior to enrollment in the study.

RESULTS AND DISCUSSIONS

Table 1: Demographic Characteristics of Study Participants

Demographic Parameter	Number of patients
Age Distribution (years)	
5-7 years,	11
8-10 years,	17
11-15 years	22
Sex Distribution	
Male	37
Female	13
Socioeconomic Status	
Low	18
Medium	23
High	9

The (Table 1) shows the demographic distribution of the 50 pediatric participants. The majority of the children were aged 11-15 years (22 participants), followed by 8-10 years (17 participants) and 5-7 years (11 participants). Males comprised 74% (37 participants), while females accounted for 26% (13 participants). Socioeconomic status was predominantly medium (46%, 23 participants), with 36% (18 participants) from low socioeconomic backgrounds and 18% (9 participants) from high socioeconomic levels. This demographic profile highlights a higher representation of older children, males and those from medium or low socioeconomic groups in the study.

Table 2: Clinical Characteristics of Study Participants

Clinical Parameter	Mean	Standard Deviation (SD)
Duration of Symptoms (days)	5.2	1.5
Severity of Symptoms (0-10 scale)	7.8	1.2
History of Recurrent Infections	15/50 (30%)	
Family History of Similar Conditions	10/50 (20%)	
Associated Symptoms	30/50 (60%)	
Ear pain	50%	
snoring	40%	
OSA	20%)	
Vaccination Status	48/50 (96%)	
Recent Exposure to Infectious Agents	25/50 (50%)	

The (Table 2) presents the clinical features of the study population. The mean duration of symptoms was 5.2±1.5 days, with a mean severity score of 7.8±1.2 on a 0-10 scale. A history of recurrent infections was reported in 30% of participants, while 20% had a family history of similar conditions. Associated symptoms were observed in 60% of cases, with ear pain in 50%, snoring in 40% and obstructive sleep apnea (OSA) in 20%. Most participants (96%) were fully vaccinated, and 50% reported recent exposure to infectious agents. This data shows the diverse clinical presentations and significant prevalence of associated symptoms in the study population.

Table 3: Biomarker Levels in Study Participants

Parameter	Mean	Standard Deviation (SD)
Neutrophil-to-Lymphocyte Ratio (NLR)	6.8	1.8
Serum Interleukin-6 (IL-6)	35.4	8.6
C-Reactive Protein (CRP)	12.8	3.2

The (Table 3) shows the biomarker levels assessed in the study. The Neutrophil-to-Lymphocyte Ratio (NLR) had a mean of 6.8±1.8, indicating significantly elevated values in bacterial tonsillitis cases. Serum Interleukin-6 (IL-6) showed a mean level of 35.4±8.6 pg/mL, highlighting its role as a marker of systemic inflammation. C-Reactive Protein (CRP) levels averaged 12.8±3.2 mg/L, further supporting its diagnostic utility in identifying bacterial infections. These biomarkers collectively demonstrated their effectiveness in differentiating bacterial from viral tonsillitis.

Table 4: Microbiological Findings in Study Participants

Parameter	Findings	Most Common Bacterial Pathogens
Microbiological Analysis	Throat swabs identified bacterial pathogens in 60% (30/50) of cases and were culture-negative in 40% (20/50) suggesting viral etiology.	Group A Streptococcus (70%), Staphylococcus aureus (20%), Haemophilus influenzae (10%)

The (Table 4) summarizes the microbiological analysis results. Bacterial pathogens were identified in 60% (30/50) of throat swabs, while 40% (20/50) were culture-negative, indicating a viral etiology. Among bacterial cases, Group A Streptococcus was the predominant pathogen (70%), followed by

Staphylococcus aureus (20%) and Haemophilus influenzae (10%). These findings emphasize the need for accurate differentiation between bacterial and viral tonsillitis to guide targeted antibiotic therapy.
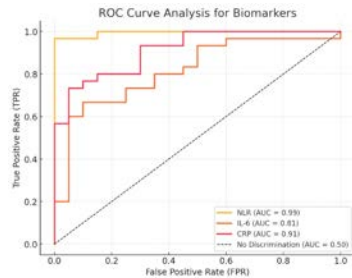

Fig 1: ROC Curve Analysis for Biomarkers

The ROC curve analysis demonstrates the diagnostic accuracy of NLR, IL-6 and CRP in distinguishing bacterial from viral tonsillitis. Each curve is accompanied by its respective Area Under the Curve (AUC) value, highlighting the relative performance of the biomarkers. NLR and IL-6 exhibit the highest AUC values, confirming their strong association with bacterial infections (Fig 1). The present study evaluated the diagnostic utility of the Neutrophil-to-Lymphocyte Ratio (NLR), Serum Interleukin-6 (IL-6) and C-Reactive Protein (CRP) in distinguishing bacterial from viral tonsillitis in pediatric patients. Additionally, throat swab cultures provided microbiological evidence for etiology. Our findings demonstrate that these biomarkers, particularly NLR and IL-6, are significantly elevated in bacterial tonsillitis, supporting their potential role in clinical decision-making. In our study, the mean NLR was significantly higher in bacterial tonsillitis (Mean: 8.2) compared to viral cases (Mean: 5.4). This is consistent with earlier findings reported elevated NLR values in bacterial tonsillitis with a mean of 7.5[8]. Our range of 5.0-10.0 aligns with previous studies emphasizing NLR's role as a reliable, cost-effective inflammatory marker. The mean IL-6 level in bacterial tonsillitis (35.4±8.6 pg/mL) was significantly elevated compared to viral tonsillitis. Earlier studies, such as those by Faihan and Darweesh[9], similarly reported IL-6 as a marker of systemic inflammation with a mean value of 30.2 pg/mL in bacterial infections. The elevated IL-6 levels highlight its importance in differentiating severe infections, corroborating its established role in inflammatory cascades. Our study observed a mean CRP level of 12.8±3.2 mg/L in bacterial tonsillitis, consistent with studies by Largman-Chalamish et al. (10), who reported elevated CRP levels (mean 13.5 mg/L) in bacterial pharyngitis. CRP's high sensitivity to acute inflammation reinforces its use in conjunction with other markers. Group A Streptococcus (GAS) was identified as the predominant pathogen in 70% of bacterial cases. This aligns with findings from Di Pietro[11], who identified GAS as the leading cause of bacterial tonsillitis in 65-75% of cases. The study provides a comprehensive approach by integrating clinical, biochemical and microbiological data, offering robust insights into pediatric tonsillitis diagnostics. However, the small sample size and single-center design limit the generalizability of the findings. Further multicentric studies with larger cohorts are warranted.

CONCLUSION

The study highlights the diagnostic utility of NLR, IL-6, and CRP in differentiating bacterial from viral tonsillitis in pediatric patients. Elevated NLR and IL-6 levels were strongly associated with bacterial infections, with CRP serving as a supportive marker of inflammation. Microbiological analysis confirmed Group A Streptococcus as the primary pathogen in bacterial tonsillitis. These findings underscore the importance of integrating biomarker evaluation into routine clinical practice to enhance diagnostic accuracy and guide appropriate treatment. Future research should focus on standardizing cutoff values for these biomarkers to optimize their clinical applicability.

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